

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

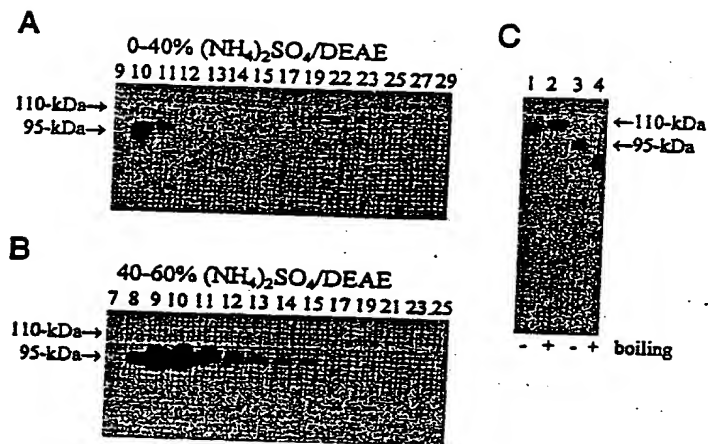


FIG. 1

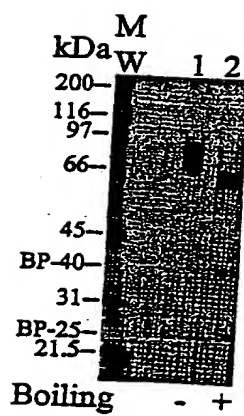


FIG. 2

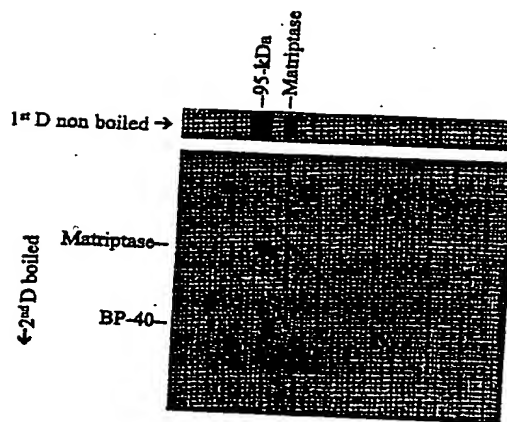


FIG. 3

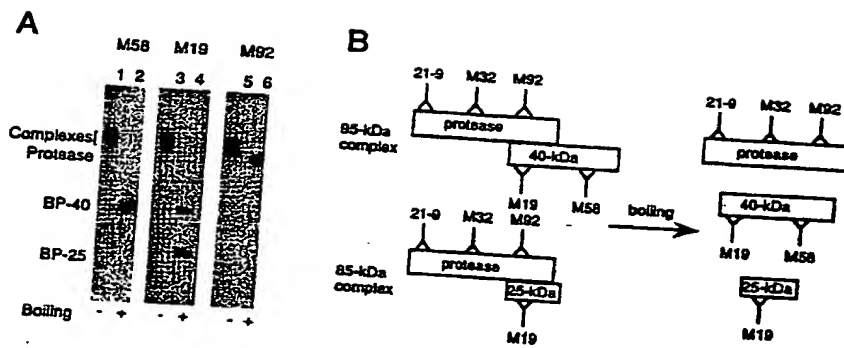


FIG. 4

1 MAPARTMARARLAPAGIPAVALWLLCTLGLOGTOAGPPPA
 41 PPGLPAGADCLNSFTAGVPGFVLDTNASVNGATFLESPT
 81 VRRGWDCVRACCTTQNCMLALVELQPDREGDAIAACFLIN
 121 CLYEQNFVCKFAPREGFINYLTRVRSYRQLRTQGFEGGS
 161 GIPKAWAGIDLKVOPOEPLVLKQVENTDWRLLRGDTDRV
 201 ERKDPNOVELWGLKEGTYLPQLTVTSSDHPEDTANVTVT
 241 LSTKQTEDYCLASNKVGRCRGSFPRWYDPTQICKSFVY
 281 GGCLGNKNYLRREECILACRGVOGFSMERHRHPVCSGTCQ
 321 PTQFRCSNGCCIDSFLECDTFCNCPDASDEAAACEKYSGF
 361 DELQRIHFPSDKGHCVDLPDTGLCKESI PRWYYNFFSEHC
 401 ARFTYGGCYGNKNNFEEQQLCSRGISKKDVFGLRREI
 441 PIPSDGSVEMAVVFLVICIVVVAILGYCFFKNQRKDFH
 481 GHHPPTPASSTVSTTEDTEHLVYNHTTRPL

FIG. 5

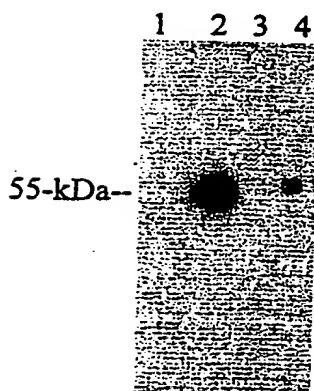


FIG. 6

0936333-030500

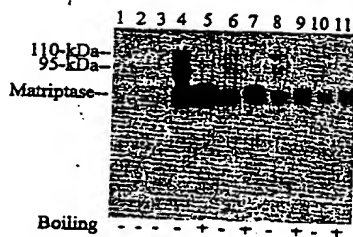


FIG. 7

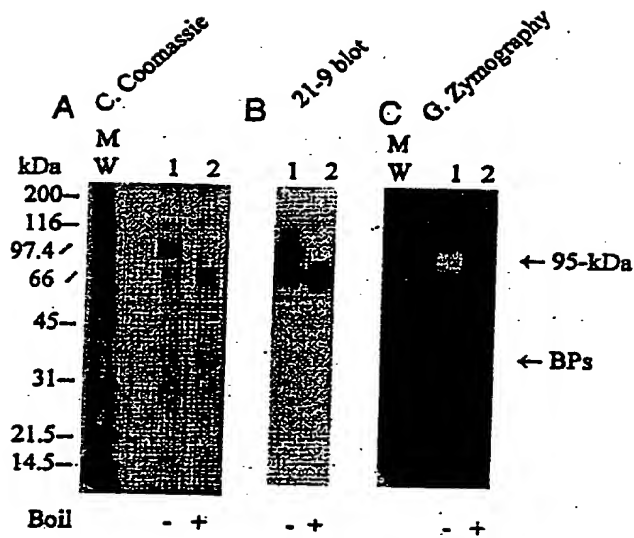


FIG. 8

-357 CGCTGGGTGTGCTGCGACGGCTGCTGATCGGCTCTCTTGGTCTTCTGGGATCGGCTCTCGGTGTGGCATTTGCGATACCGG
 -270 GAGTGTGCTGTGTCACAGGCTCTCAATGGCTACATGAGGATACAAATGAGAAATTTTGGATGCTCAGAGAAATCCAACCTCAGTACGG
 -180 TTGTAAAGCTTGCCACAGGCTGAAGGACGGCTGAAGCTGCTGACGGGAGTCCATTCTGGGCGCTTACCACAGGAGATCGGCT
 -90 GTGACGGGCTTCAAGGACGGGACGGCTGATCGGCTACTGCTGCTGAGTTGACGATCCCGACAGCACTGGTGAGGAGGGCGGACGGCTC
 1 ATGCGCAGGAGCGGCTAGTCATGCTGCGCGGGCGGCTCTCAAGTCTTTGGTCACTCAGTGGTGGCTTTCCCGACGAG
 1 M A E E R V V K L P P R A R S L K S V F V T S V Y A F P T D
 91 TCEAAAACAGTACAGAGGACCCAGGACAACAGCTGCAGCTTTGGCTGACGCGCGCGGTGTGAGCTGATGCGCTTACCACGCGCGG
 31 S K T V Q R T O D N S C S F G G L H A R G V E L H R F T C C T T P G
 181 TTCCCTGACAGCCCCCTACCCGCTCATGCCGCTGCGAGTGGGCCCTCGCGGGGACCCGAGCTCAGTGTGAGCCTCAGCTTCCCGACG
 61 F P D S P Y P A H A R C Q W A L R G D A D S V L S L T F R S
 271 TTGACCTTGGCTCTCGACGAGCGCGGACGACCTGGTGACGGTGTAACAACCTGAGCCCCATGAGAGCCCAAGCGGCTGGTGAG
 91 F D L A S C D E R G S D L Y T V Y N T L T S P H E P H A L V Q
 381 TTGTGTGGCACTACCTCTCTCTACAACCTGACTTCCACTCTCCCAAGCTCTGCTCATACATGATAACCAACATCAGGCG
 121 L C G T Y P P S Y N L T F H S S Q N V L L I T L I T N T E R
 451 CGGCATCCCGCTTTCAGGCCACCTTCTTCAGCTGCTAGGATGAGCAGCTGTGGAGGCGGCTTACGTAAGAGCCAGGGGACATTCAAC
 151 R H P G F E A T F F Q L P R H S S C G G R L R K A D G G T F N
 541 AGCCCTTACTACCGGCGCACTACCCACCCCAACATGACTGCACATGGAACATGAGGTGCCCAACACAGCATGGAAGTCCGCTTC
 181 S P Y Y P G H Y P P N I D C T W N I E V P N N Q H V Y R F
 830 AAATTCTTCTACCTGCTGGAGCCCGGCTGCTCGGGGACCTGCCCAAGGACTACGTGGAGATCAATGGGAGAAATCTGCGGAGAG
 211 K F F Y L L E P G V P A G T C P K D Y V E I N G E K Y C G E
 721 AGGTCCGAGTTCGTCGTACCCAGCAACAGCAACAGATCACAGTTCGCTTCCACTCAGATCAGTCTACACGACACCGGCTTCTTAGCT
 241 R S Q F V Y T S N S N K I T V R F M S D Y S T D T G E F L A
 811 GAATACCTTCTCTACGACTGACCTGACCCATGCGCGGGGAGTTCAGTGTGCGACGGGCGGTGTCTCGGAAGCAGCTGCGCTGTGAT
 271 E Y L S Y D S S O P C P G O F T C T R C T G C I R K E L R C D
 901 GGCTGGCGGACGACCCGACCAACAGCATGAGCTCAACTGCACTGCGACGCGGGGACAGTTCAGTGTCAAGAACAAAGTTCTGCAAG
 301 G W A D C T D H S S D E L N C S C D A G H O F T C K N K F C K
 991 CCCCCTTCTGGGCTTCCGACAGTGTGAACGACTGCGGAGACAACAGCGAGCAGCAGGAGTGTGCTCGGCGGACAGCTTTCAGGTGT
 331 P L F V V C D S V N D C G G D N S D O G G C S C P A O T F R C
 1081 TCCATGSGGAAGCTCTCTCBAASAGCCAGCAGTGCATAGGGAAGGAGCACTGTGGGACGGTCCGACAGGCGCTCTCGCCCAAGGTG
 361 S N G K C L S K S S Q C G G A D D C G D G S D E A S C P K V
 1171 AACGTCGTCACCTTGATCCAAACACACCTACCGCTGCTCTCAATGGGCTCTGCTTGAGCAAGGGCAACCTGAGTGTGACGGGAAGGAGGAC
 391 N V Y T C T K H T Y R C L N G L C T L S K G N P E C D G K E D
 1261 TGTACCCAGCGCTCAGATGAGAAGGACTGCACTGTGGGCTGCGGCTATTACGAGACAGGCTCGTGTGTTGGGGGACGGATGCGGAT
 421 C S D G S D E K D C D C G L R S F T R O A R V Y G G G T D K O
 1351 GAGGGCAGTGGCCCTGGGAGGTAAGCCTGCATGCTTGGGCGAGGCACTGCGGCTGCTTCCCTCATCTCTCCCAACTGGCTGGTC
 451 E G E G V W D V S L H A L G Q G G G C A C T G C G A S L I S P N W L V
 1441 TGTGCGGCACTGCTACATCGATGACAGAGGATTCAGGTACTCAGACCCACGCGAGTGGAGCGGCTTCTGGGCTTGACGACGAGAGG
 481 S A A H C Y I D R G F R Y S D P T Q W T A F L G L H D Q S
 1531 CAGCGACGCGCCCTGGGCTGAGGAGGCTGAGGCTATCATCTCCACCCCTTCTTCAATGACTTCACCTTCAGCTATGACATC
 511 Q R S A P G V O E R R L K R I S H P F F N D G T F D Y I I
 1621 CGCTGCTGAGGCTGAGAAACCGGACAGATACAGCTCCATGGTGGGCGCATCTGCGCTGCGGAGCGCTCCCATGTCTTCCCTGCGCGG
 541 A L L E L E K P A E Y S S H V R P I C L P D A S H V F P A G
 1711 AAGGCCATCTGGGCTCAGGCTGGGACACACCCAGTATGAGGAGCAGTCTGCGGCTGATCTGCAAAAGGGTGAGATCGGCTCAGCTCAAC
 571 K A I W V J G W G H T Y G G T G A L I L O K G E I R V I N
 1801 CAGACCACTGCGAGAACCTCTGCGCGACAGATCAGCGCGGCGATGTGCGCTGGGCTTCTCAGCGGCGGCTGAGCTCTGCGCAG
 601 Q T T C E N L L P Q O I T P R N H M C V G F L S G G G V D S C O
 1891 GGTATTCCGGGGACCCCTGTGCGAGCTGGAGGCGGATGGCGGATCTTCCAGCCCGGCTGGTGGTGGGAGGAGCGGCTGCGCTCAG
 631 G D S G P L S S V E A D R I F O A G V V S W G D G C A G
 1981 AGGAACAAGCAGGCGGTGATACAAAGGCTCCCTCTGTTTGGGACGATCAAAAGAGAACACTGGGATAGAGGCGCGGGGACCCCAAA
 681 R N K P G V Y T R L P L F R D V I K E N T G V ---
 2071 TGTGTACACCTCGGGGGCCACCCATCGTCCACCCTAGTGTGACCGCTGCGAGCTGGAGACTGGACCTGACCTGACACGCGGCGGCGG
 2181 AACATCACTGTAACTCAATCTCAGGGCTCCAAATGCTGCAAGAAACCTCTGCTTCTTCCAGCCTCCAAAGTGGAGCTGGGAGTAG
 2251 AAGGGAGAGGACTGGGTTCTACTGACCCCACTGGGGGCAAGGTTTGAAGACAGAGCTTCCCGGCGAGCCCAAGCTGGGCGGAGG
 2341 CCGGTTTGTGATATGCTGCTTCCCTTGTCTGAAGGACGACGGGACGAGGCTTCCGAGCTTCTCAGTGAAGGTTGGTGGGCTGCGG
 2431 ATCTGGGCTGTGGGCTTGGGCGACGCTCTGTGAGGAAGCCAGGCTCGGAGGACCTGGGAACACAGCGGCTTGGAGACTGAAATG
 2521 TTACAGACTCCCAAGTGACTTCAGTGTGTATGTGTAAATGAGTAAACATTTTATTTCTTTTAAAAAATGAG

FIG. 9

[illegible][illegible]

FIG. 10

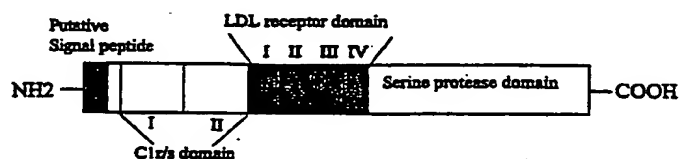
A LDL-receptor type regions

Matriptase (280-314)	PCPG--QFTICRTGRCKIRKELR-CDGWADCTDHSDELNC
(315-351)	SCDAGHQFTICKNKFCCKPLFWV-CDSVNDCGDNSEDQGC
(352-387)	SCPA-QTERCSNGKCLSKSQ-CCNGKDDCGDGSDEASC
(394-430)	TCTK-HTYRCLNGLCLSKGNPECCKGKEDCSGDSDEKDC
Consensus sequences	
LDL-receptor	TC....EF..C..G..CI...W..-CD...DC..DGSDE..C
LRP	.C....-F..C....RCIP..W..-CDG..DC..D..SDE..C
Perlecan	PC..P..EF..C....C....-CD...DC..D..SDE..C
GP-330	.C....-F..C....CI.....-CDG..DC..DGSDE..C

B C1r/s type region

Mt (1) 42	CSGLHARGVELMRFTTPGFFDSPPYPAHARQWALRGDADSVLSLTFRS--EDLASCDERGSDLV
Mt (2) 168	CGRLRKAQ-ET--FNSHYFG-HYPPNIDITWNEVPNNOHVKVRF-KFFYLLEPGVPAGT--D
C1r (2) 193	CSSELYTEASGY--ISSLEYPR-SYPPDLRCNYSIRVERGLTLHLKFL-EPFDIDD-HQOVH--D
C1s (2) 175	CSGDVFTALIGE--IASPNYPK-PYPENSRCFYQIRLEKGFQVVVTLRREDQVEAADSAGN--D
RaRF (2) 185	CDNLFTORTGV--ITSDFPN-PYPKSSECLYTHELEEGFMVNLQFE-DIFDIED-HPEVP--D
CSP (2) 181	CSGDVFTALIGE--IASPNYPK-PYPENSRCFYQIRLEKGFQVVVTLRREDQVEAADSAGN--D

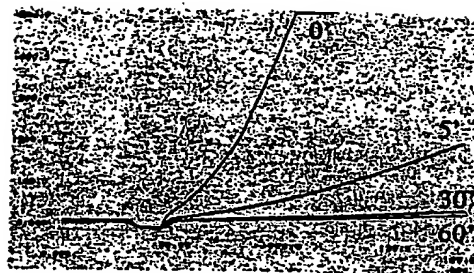
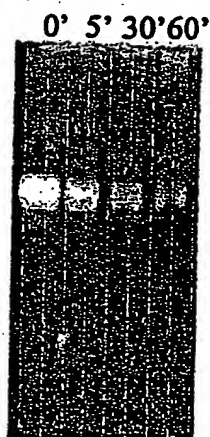
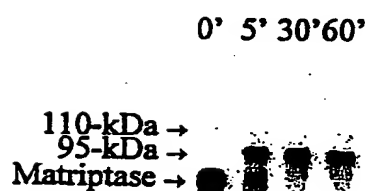
Mt (1) 107	VYNTLS-PHEPHALVQLCQTYFSSYNLTFHSSQVLLITLITNTERRHGF	155
Mt (2) 226	PKDYVEINGE-----YCGER--IS-QFVVTSNSNKITVRPHSDQSYTDIG	268
C1r (2) 251	PYDLQIYANGKNIGFCGXORPP-DLD--TSSNAVOLLFFIDESGDSRGW	298
C1s (2) 235	L-DSLQVAVAGDROFGPYCGHGFG-PLNIETKSNALDIIFOTDLTGOKKGW	283
RaRF (2) 243	PYDIYIKYVGPVKVLGPFCEKAFEPIS--TQSHSVLIUHSNNGENRGW	290
CSP (2) 241	Q-DSLFAAKNRQFGPFCEGFG-PLTIETHSNITLOIVEOTDLTEQKKGW	289

FIG. 11**FIG. 12**

A. Immunoblot

B. G. Zymogram

C. Fluorimetric Assay



	Cleavage Rate ¹	Residual Rate
0 min.	725	100%
5 min.	114	18%
30 min.	17	2.3%
60 min.	13	1.8%

FIG. 13

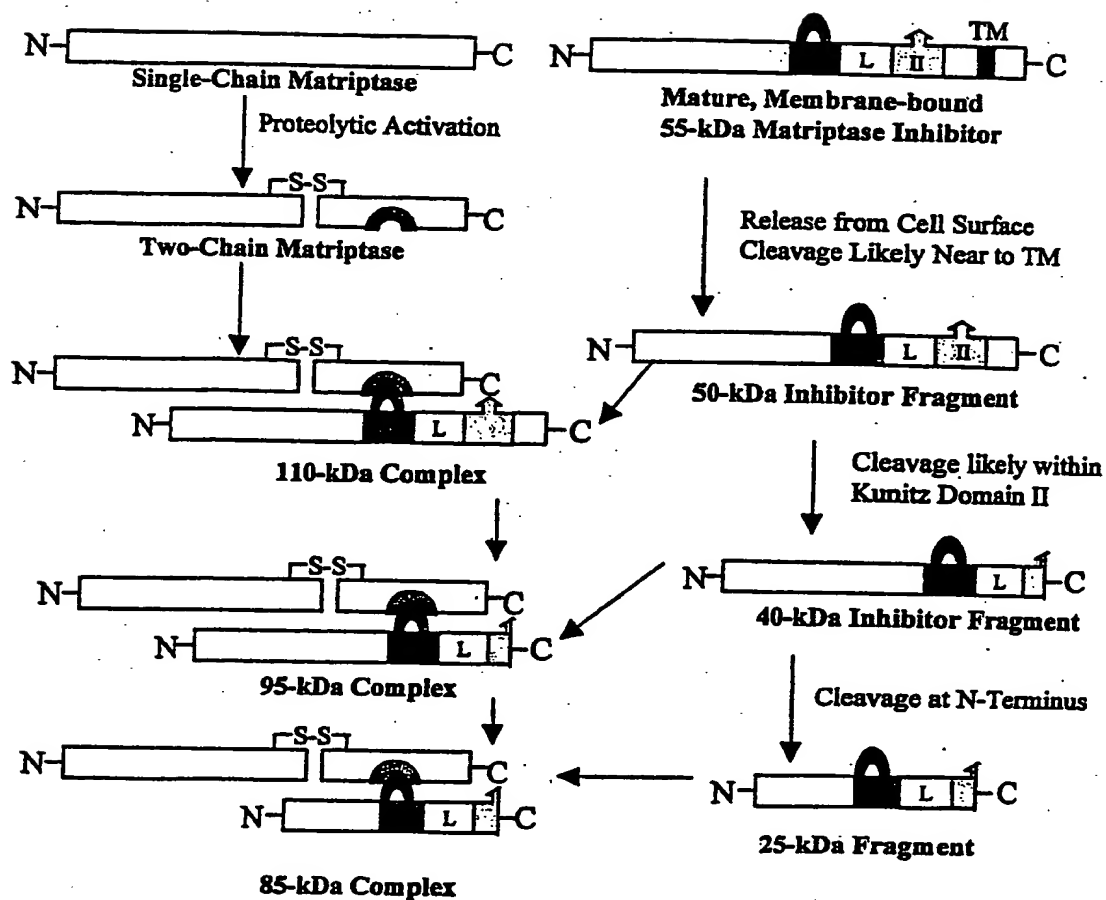


FIG. 14

1 gacgcctgtg agaccgcgca gcggcctcgg ggaccatggg gagcgatcgg gcccgcaagg
61 gcggagggggg cccgaaggac ttcggcgcg gactcaagta caactcccgg cacgagaaaag
121 tgaatggcctt ggaggaaggc gtggagttcc tgccagtcag caacgtcaag aaggtggaaa
181 agcatggccc ggggcgctgg gtggtgctgg cagccgtgct gatcgccctc ctcttggtct
241 tgctggggat cggcttcctg gtgtggcatt tgcagtaccg ggacgtgctg gtccagaagg
301 tcttcaatgg ctacatgagg atcacaatg agaattttgt ggatgcctac gagaactcca
361 actccactga gtttgtaagc ctggccagca aggtgaagga cgcgctgaag ctgctgtaca
421 gcggagtcctt attcctgggc cctaccaca aggagtcggc tgtgacggcc ttcagcgagg
481 gcagcgtcat cgcctactac tgggtctgagt tcagcatccc gcagcacctg gtggaggagg
541 ccgagcgcgt catggccgag gagcgcgtag tcatgctgcc cccgcggggc cgtccctga
601 agtcctttgt ggtcacctca gtggtggctt tccccacgga ctccaaaaca gtacagagga
661 cccaggacaa cagctgcagc tttggcctgc acgcccgcgg tgtggagctg atgcgcttca
721 ccacgcccgg cttccctgac agcccctacc ccgctcatgc ccgctgccag tgggcccctgc
781 ggggggacgc cgactcagtg ctgagcctca ccttcgcag ctttgacctt gcgtcctgcg
841 acgagcgcgg cagcgacctg gtgacggtgt acaacaccct gagccccatg gagccccacg
901 ccctggtgca gttgtgtggc acctaccctc cctcctacaa cctgaccttc cactcctccc
961 agaacgtcct gctcatcaca ctgataacca acactgagcg gcggcatccc ggctttgagg
1021 ccaccttctt ccagctgcctt aggatgagca gctgtggagg ccgcttacgt aaagcccagg
1081 ggacattcaa cagcccctac taccaggcc actaccacc caacattgac tgcacatgga
1141 acattgaggt gcccaacaac cagcatgtga aggtgcgctt caaattcttc tacctgctgg
1201 agcccggcgt gcctgcgggc acctgccccca aggactacgt ggagatcaat ggggagaaat
1261 actgcgagga gaggtcccag ttcgtcgtca ccagcaacag caacaagatc acagttcgct
1321 tccactcaga tcagtcctac accgacaccg gcttcttagc tgaatacctc tcctacgact
1381 ccagtacccc atgcccgggg cagttcacgt gccgcacggg gcggtgtatc cggaaggagc
1441 tgcgctgtga tggttggggc gactgcaccg accacagcga tgagctcaac tgcagttgcg
1501 acgcccggcca ccagttcacg tgcaagaaca agttctgcaa gcccctcttc tgggtctgcg
1561 acagtggtgaa cagctgcgga gacaacagcg acgagcaggg gtgcagttgt ccggcccaga
1621 ccttcaggtg ttccaatggg aagtgcctct cgaaaagcca gcagtgaat gggaaggagc
1681 actgtgggga cgggtccgac gaggcctcct gcccgaaggt gaacgtcgtc acttgtacca
1741 aacacaccta ccgctgcctc aatgggctct gcttgagcaa gggcaaccct gagtgtgacg
1801 ggaaggagga ctgtagcgac ggctcagatg agaaggactg cgactgtggg ctgcggtcat
1861 tcacgagaca ggctcgtgtt gttgggggca cggatgcgga tgagggcgag tggccctggc
1921 aggtaagcct gcatgctctg ggccaggggc acatctgcgg tgcttccctc atctctccc
1981 actggctggt ctctgcgca cactgctaca tcgatgacag aggattcagg tactcagacc
2041 ccacgcagtg gacggccttc ctgggcttgc acgaccagag ccagcgcagc gccctgggg
2101 tgcaggagcg caggctcaag cgcctcatct cccaccctt cttcaatgac ttcacctcg
2161 actatgacat cgcgctgctg gagctggaga aaccggcaga gtacagctcc atggtgcggc
2221 ccatctgcct gccggacgcc tccatgtct tccctgccgg caaggccatc tgggtcacgg
2281 gctggggaca caccagtat ggaggcactg gcgcgctgat cctgcaaaag ggtgagatcc
2341 gcgtcatcaa ccagaccacc tgcgagaacc tcctgccgca gcagatcacg ccgcgcatga
2401 tgtgcgtggg cttcctcagc ggcggcgctg actcctgcca ggggtattcc gggggacccc
2461 tgtccagcgt ggaggcggat gggcggtatc tccaggccgg tgtggtgagc tggggagacg
2521 gctgcgctca gaggaacaag ccaggcgtgt acacaaggct ccctctgttt cgggactgga
2581 tcaaagagaa cactggggta taggggcccgg ggccacccaa atgtgtacac ctgcggggccc
2641 acccatcgtc caccacagtg tgcacgcctg caggctggag actggaccgc tgactgcacc
2701 agcgccecca gaacatacac tgtgaactca atctccaggg ctccaaatct gcctagaaaa
2761 cctctcgctt cctcagcctc caaagtggag ctgggaggta gaaggggagg aactggtgg
2821 ttctactgac ccaactgggg gcaaagggtt gaagacacag cctccccgc cagccccaag
2881 ctggggccgag gcgcgtttgt gtatatctgc ctcctctgtc tgtaaggagc agcgggaacg
2941 gagcttcgga gcctcctcag tgaagggtgt ggggctgccg gatctgggct gtggggccct
3001 tggggccagc tcttgaggaa gccaggctc ggaggaccct ggaaaacaga cgggtctgag
3061 actgaaaatg gtttaccagc tcccaggta cttcagtggt tgtattgtgt aaatgagtaa
3121 aacattttat ttctttttaa aaaaaaaaa

FIG. 15

1 mgsdrarkgg ggpkdfigagl kynsrhekv n gleegveflp vnnvkkvekh gpgrwvvlaa
61 vliglllvll gigflvwhlq yrdvrvqkvf ngymritnen fvd dayensns tefvslaskv
121 kdalkllysg vpflgpyhke savtafsegs viayywsefs ipqhlveeae rvmaeervvm
181 lpprarslks fvtvsvvafp tds ktvqrtq dnscsfglha rgvelmrftt pgfpdspypa
241 harcqwalg dadsvlsltf rsfdlascde rgsdlvtvyn t lspmephal vqlcgytpps
301 ynltfhssqn vllitlitnt errhpgfeat ffqlprmsc ggrrlkaagt fnsppypghy
361 ppnidctwni evpnnqhvkv rfkffyllep gvpagtcpkd yveingekyc gersqfvvts
421 nsnkitvrfh sdqsytdtgf laeysydss dpcpgqftcr tgrcirkelr cdgwadctdh
481 sdelncsda ghqftcknkf ckplfwvcds vndcgdnsde qgcscpaqtf rcsngkclsk
541 sqqcngkddc gdgsdeascp kvnvtctkh tyrclnglcl skgnpecdgk edcsdgsdek
601 dcdcglsrft rgarvvggtd ad egewpwqv slhalggghi cgaslispnw lvsaahcyid
661 drgfrysdpt qwtaflglhd qsqr sapgvq errlkriish pffndftfdy diallelekp
721 aeyssmvrpi clpdashvfp agkaiwvtgw ghtqygg tga lilqkgeirv inqttcenll
781 pqqitprmmc vgflsggvds cggdsggpls sveadgrifq agvvswgdgc aqrnkpgvyt
841 rlp lfrdwik entgv

FIG. 16

2050E0*EE9E660

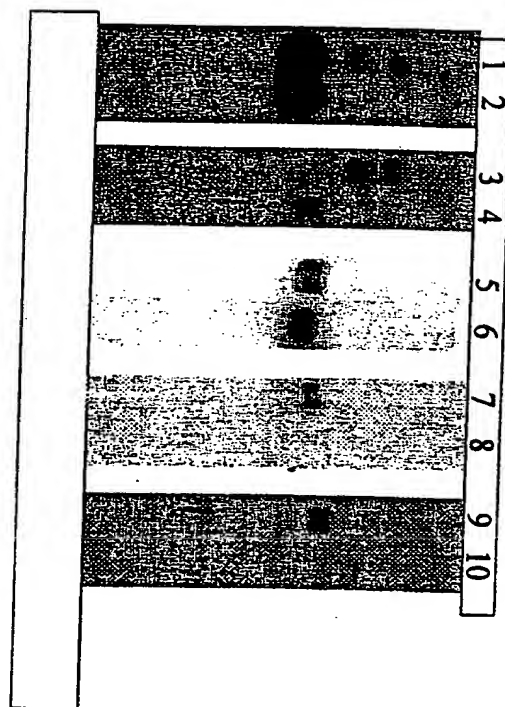


FIG. 17

09936333.030502